Biodegradable Polymeric Nanoparticles: Drug Delivery Systems-A Review

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Abstract

Biodegradable nanoparticles have been used frequently as drug delivery vehicles due to its grand bioavailability, better encapsulation, control release and less toxic properties. Various nanoparticulate systems, general synthesis and encapsulation process, control release and improvement of therapeutic value of nanoencapsulated drugs are covered in this review. We have highlighted the impact of nanoencapsulation of various disease related drugs on biodegradable nanoparticles such as PLGA, PLA, chitosan, gelatin, polycaprolactone and poly-alkyl-cyanoacrylates.

Key words: Nanoparticles, PLGA, PLA, chitosan, gelatin, polycaprolactone

Introduction

Biodegradable nanoparticles are frequently used to improve the therapeutic value of various water soluble/insoluble medicinal drugs and bioactive molecules by improving bioavailability, solubility and retention time. These nanoparticle–drug formulation reduces the patient expenses, and risks of toxicity. Nanoeapsulation of medicinal drugs (nanomedicines) increases drug efficacy, specificity, tolerability and therapeutic index of corresponding drugs. These nanomedicines have many advantages in the protection of premature degradation and interaction with the biological environment, enhancement of absorption into a selected tissue, bioavailability, retention time and improvement of intracellular penetration. Several disease related drugs/bioactive molecules are successfully encapsulated to improve bioavailability, bioactivity and control delivery. Nanomedicine formulation depends on the choice of suitable polymeric system having maximum encapsulation (higher encapsulation efficiency), improvement of bioavailability and retention time. These drug nanof ormulations (nanodrug) are superior to traditional medicine with respect to control release, targeted delivery and therapeutic impact. These targeting capabilities of nanomedicines are influenced by particle size, surface charge, surface modification, and hydrophobicity.
Among these, the size and size distributions of nanoparticles are important to determine their interaction with the cell membrane and their penetration across the physiological drug barriers. The size of nanoparticles for crossing different biological barriers is dependent on the tissue, target site and circulation. For the cellular internalization of the nanoparticles, surface charge is important in determining whether the nanoparticles would cluster in blood flow or would adhere to, or interact with oppositely charged cells membrane.

**Fig.** Type of biodegradable nanoparticles: According to the structural organization biodegradable nanoparticles are classified as nanocapsule and nanosphere. The drug molecules are either entrapped inside or adsorbed on the surface.

**Synthesis and encapsulation of drugs in polymeric nanoparticles**
Polymeric nanoparticles have been synthesized using various methods according to needs of its application and type of drugs to be encapsulated. These nanoparticles are extensively used for the nanoencapsulation of various useful bioactive molecules and medicinal drugs to develop nanomedicine. Biodegradable polymeric nanoparticles are highly preferred because they show promise in drug delivery system. Such nanoparticles provide controlled/sustained release property, subcellular size and biocompatibility with tissue and cells. Apart from this, these nanomedicines are stable in blood, non-toxic, non thrombogenic, non immunogenic, non inflammatory, do not activate neutrophils, biodegradable, avoid reticuloendothelial system and applicable to various molecules such as drugs, proteins, peptides, or nucleic acids. The general synthesis and encapsulation of biodegradable nanomedicines are represented in Fig. The drug molecules either bound to surface as nanosphere or encapsulated inside as the most commonly and extensively used polymeric nanoparticles (poly-d,l-lactide-co-glycolide, polylactic acid, poly-_,caprolactone, poly-alkyl-cyanoacrylates, chitosan and gelatin), their therapeutic advantages, general synthesis and encapsulation of various disease related drug have been described in this part of the review.

**Poly-d,l-lactide-co-glycolide (PLGA)**
PLGA (poly-d,l-lactide-co-glycolide) is one of the most successfully used biodegradable nanosystem for the development of nanomedicines because it undergoes hydrolysis in the body to produce the biodegradable metabolite monomers, lactic acid and glycolic acid. Since the body effectively deals with these two monomers, there is very minimal systemic toxicity associated by using PLGA for drug delivery or biomaterial applications. PLGA nanoparticles have been mostly prepared by emulsification–diffusion, solvent emulsion–evaporation, interfacial deposition and nanoprecipitation method.

**Polyactic acid (PLA)**
PLA (polylactic acid) polymer is biocompatible and biodegradable material which undergoes scission in the body to monomeric units of lactic acid as a natural intermediate in carbohydrate metabolism. PLA nanoparticles have been mostly prepared by solvent evaporation, solvent displacement, salting out and solvent diffusion. The salting out procedure is based on the separation of a water miscible solvent from aqueous solution by adding salting out agent.
like magnesium chloride, calcium chloride, etc. The main advantage of salting out procedure is that it minimizes stress to protein encapsulants.

**Poly-\(-\)-caprolactone (PCL)**

PCL (poly-\(-\)-caprolactone) is degraded by hydrolysis of its ester linkages in physiological conditions (such as in the human body) and has therefore received a great deal of attention for use in drug delivery. In particular, it is especially interesting for the preparation of long-term implantable devices, owing to its degradation slower than that of polylactide. PCL nanoparticles have been prepared mostly by nanoprecipitation, solvent displacement and solvent evaporation. We are describing below some of the molecules that have been successfully incorporated into PCL nanoparticles to increase their therapeutic value.

**Chitosan**

Chitosan is a modified natural carbohydrate polymer prepared by the partial N-deacetylation of crustacean derived natural biopolymer chitin. There are at least four methods reported for the preparation of chitosan nanoparticles as ionotropic gelation, microemulsion, emulsification solvent diffusion and polyelectrolyte complex. Ionotropic gelation is based on electrostatic interaction between amine group of chitosan and negatively charge groups of polyanion such as tripolyphosphate. Chitosan is dissolved in acetic acid in the absence or presence of stabilizing agent. Polyanion was then added and nanoparticles were spontaneously formed under mechanical stirring.

**Gelatin**

Gelatin is extensively used in food and medical products and is attractive for use in controlled release due to its nontoxic, biodegradable, bioactive and inexpensive properties. It is a polyampholyte having both cationic and anionic groups along with hydrophilic group. It is known that mechanical properties, swelling behavior and thermal properties depend significantly on the crosslinking degree of gelatin. Gelatin nanoparticles can be prepared by desolvation/coacervation or emulsion method. Desolvation/coacervation is a process during which a homogeneous solution of charged macromolecules undergoes liquid–liquid phase separation, giving rise to a polymer rich dense phase at the bottom and a transparent solution above. The addition of natural salt or alcohol normally promotes coacervation and the control of turbidity/crosslinking that resulted in desired nanoparticles. Many encapsulants have been successfully encapsulated into gelatin nanoparticles.

**Poly-alkyl-cyano-acrylates (PAC)**

The biodegradable as well as biocompatible poly-alkylcyanoacrylates (PAC) are degraded by esterases in biological fluids and produce some toxic products that will stimulate or damage the central nervous system. Thus this polymer is not authorized for application in human. However, PAC nanoparticles are prepared mostly by emulsion polymerization, interfacial Polymerization and nanoprecipitation for drug delivery and nanoformulation. Emulsion polymerization is classified into two categories based on the use of an organic or aqueous continuous phase. An advantage of interfacial polymerization technique is high efficiency drug encapsulation. Table shows some of the biodegradable polymer efficiently used for nanoformulations as shown below.

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Conclusion

Nanoparticulate drug delivery systems seem to be a viable and promising strategy for the biopharmaceutical industry. They have advantages over conventional drug delivery systems. They can increase the bioavailability, solubility and permeability of many potent drugs which are otherwise difficult to deliver orally. Nanoparticulate drug delivery systems will also reduce the drug dosage frequency and will increase the patient compliance. In near future nanoparticulate drug delivery systems can be used for exploiting many biological drugs which have poor aqueous solubility, permeability and less bioavailability. Nanoparticles can minimize some of these drugs unique problems by safeguarding stability and preserving their structure.

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